REMARKS

Claims 1-23 are pending. Claim 23 is amended herein to place it in independent form. No new matter is added.

Previous Rejections under 35 U.S.C. § 103

Claims 1-22 were rejected as allegedly being obvious in view of the combination of O'Hare et al. (WO 97/05265), in combination with Hawley- Nelson et al. (U.S. Patent No. 6,376,248), Schwartz et al. (U.S. Patent No. P 6,034,135), and Moyer et al. (U.S. Patent 5,935,777). Applicants respectfully disagree with this rejection.

None of the cited documents when read alone or in combination suggest the type of VP22 containing aggregates of the pending claims. VP22 containing aggregates are clearly defined in the specification as "associations of molecules forming particles" (e.g. see the specification at page 2, line 22). In addition, one of skill in the art would not be motivated, based on these documents to produce this type of claimed VP22 aggregate.

Specifically, O'Hare et al. (WO 97/05265) mentions a VP22 polypeptide attached to another molecule to be transported. However, these are not the "aggregated particles" of the present disclosure. Indeed, WO 97/05265 makes no mention or suggestion of any such aggregated particles.

Schwartz et al. (U.S. Patent No. 6,034,135) does mention aggregates. However, the aggregates disclosed in Schwartz et al. are of an entirely different nature to the aggregates presently claimed. The aggregates of Schwartz et al. comprise cationic lipids which themselves aggregate with anionic macromolecules through attraction between positively charged lipid and the negatively charged anionic macromolecule (see U.S. Patent No. 6,034,135 at column 10, line 66 to column 11 , line 10). Although claim 17 does specify presence of a liposome, the liposome merely encapsulates the already formed VP22 aggregate. Such an encapsulated aggregate is neither mentioned nor suggested in Schwartz et al.

Similarly Hawley-Nelson et al. (U.S. Patent No. 6,376,248) describes entirely different peptide-nucleic acid complexes to the aggregated particles of the present disclosure. Hawley-Nelson et al. makes bare mention of use of herpes simplex virus VP22 (column 6, line 46) as part of a very extensive and long list of proteins which are "useful in transfection compositions" (column 6, lines 27-28). Indeed, just about any type of protein (or fragment or portion thereof) would appear to fall under this extensive list (column 5, line 54 to column 6, line 64). What is described are "transfection compositions" containing any one of these proteins (or fragments or portions) or protein-lipid conjugates and nucleic acids (e.g. at column 5, lines 10-14). In all

cases the transfection agents, preferably cationic lipid compositions, are used in order to form the complexes e.g. Lipofectin etc (e.g. column 8, lines 54 to column 9, line 41). By contrast, the present disclosure is based on the observation that VP22 can, when mixed as described in the application with oligonucleotides or polynucleotides, form stable aggregated particles which can be observed by light microscopy. Hence, these claimed stable aggregated particles formed by specifically mixing VP22 protein with oligonucleotides or polynucleotides are different from the transfection complexes described by Hawley-Nelson et al.

Moyer et al. does not mention or suggest the use of any aggregates whatsoever, nor does Moyer et al. disclose the use of VP22.

In fact, the disclosure of Schwartz et al., and of Hawley-Nelson et al., in combination with O'Hare et al., teaches away from claims 1-22, since one of skill in the art would use these disclosures to make the type of complexes described in these citations, or to make the transport molecules described in O Hare et al. Moyer et al. does not make up for the deficiencies of Schwartz et al., Hawley-Nelson et al., or O'Hare et al.

Hence, Applicants respectfully submit claims 1-22 are not obvious over O' Hare et al. (WO 97/05265), alone or in combination with Hawley- Nelson et al. (U.S. Patent No. 6,376,248), Schwartz et al. (U.S. Patent No. 6,034,135), and Moyer et al. (U.S. Patent No. 5,935,777). Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

If any minor matters remain to be addressed before a Notice of Allowance is issued, the Examiner is requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By _____
Susan Alpert Siegel, Ph.D.
Registration No. 43,121

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 226-7391
Facsimile: (503) 228-9446

Marked-up Version of Amended Claims
Pursuant to 37 C.F.R. §§ 1.121(b)-(c)

In the claims:

1. (Reiterated) An aggregated composition comprising (a) a VP22 polypeptide or a fragment thereof having a transport function of VP22, and (b) an oligonucleotide or polynucleotide.

2. (Reiterated) An aggregated composition according to claim 1, which further comprises a pharmaceutically acceptable excipient.

3. (Reiterated) An aggregated composition according to claim 1, wherein the VP22 fragment comprises amino acid residues 159-301 of SEQ ID NO: 12.

4. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide comprises a circular plasmid.

5. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide comprises modified phosphodiester linkages.

6. (Reiterated) An aggregated composition according to claim 5, wherein the modified phosphodiester linkages comprise phosphorothioate linkages.

7. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide is labeled with a detectable label.

8. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide is selected from the group consisting of: an antisense molecule, a ribozyme molecule, a chimeroplast, and a polynucleotide capable of binding a transcription factor.

9. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide encodes a protein or peptide.

10. (Reiterated) An aggregated composition according to claim 1, wherein the VP22 polypeptide or fragment thereof is a fusion protein comprising a non-VP22 peptide or protein.

11. (Reiterated) An aggregated composition according to claim 10, wherein the non-VP22 polypeptide sequence is linked to the VP22 polypeptide or the fragment thereof by a cleavage-susceptible amino acid sequence.

12. (Reiterated) An aggregated composition according to claim 1, wherein the polypeptide is conjugated to a glycoside.

13. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide is coupled to a non-nucleotide molecule.

14. (Reiterated) An aggregated composition according to claim 1, wherein the aggregate comprises polypeptide and nucleotide in a ratio of at least 1 to 1.

15. (Reiterated) An aggregated composition according to claim 1, wherein the oligonucleotide or polynucleotide comprises at least about 10 bases.

16. (Reiterated) An aggregated composition according to claim 1, which comprises particles of said aggregated composition having a particle size in the range of about 0.1 to about 5 microns.

17. (Reiterated) An aggregated composition according to claim 1, wherein said polypeptide and said nucleotide are encapsulated in a liposome.

18. (Reiterated) A method of making an aggregated composition according to claim 1, comprising

(a) contacting the VP22 polypeptide, or the fragment thereof having a transport function of VP22, with an oligonucleotide or a polynucleotide, wherein said contact is in solution; then

(b) mixing the solution obtained in step (a); and

(c) incubating the mixture obtained in step (b) such that said incubation is sufficient for the VP22 polypeptide or fragment thereof to form aggregates with the oligonucleotide or polynucleotide to form aggregates.

19. (Reiterated) A method according to claim 18, wherein the polypeptide is contacted with nucleotide in a ratio of at least 1 to 1 of polypeptide to nucleotide.

20. (Reiterated) A method of delivering molecules to a cell *in vitro* comprising (a) contacting said cell with an aggregated composition according to claim 1, thereby delivering the oligonucleotide or polynucleotide to the cell.

21. (Reiterated) A cell preparation which as been treated with an aggregated composition according to claim 1.

22. (Reiterated) The method of claim 18, further comprising

(d) isolating aggregates obtained in step (c) which have a particle size of about 0.1 to about 5 microns.

23. (Amended) [The method of claim 20, further comprising] A method of delivering molecules to a cell *in vitro* comprising

(a) contacting said cell with an aggregated composition comprising a VP22 polypeptide or a fragment thereof having a transport function of VP22, and an oligonucleotide or polynucleotide, thereby delivering the oligonucleotide or polynucleotide to the cell; and

(b) exposing the cell to light, whereby said light exposure promotes disaggregation of the aggregated composition.